Assay for HCV Protease Inhibitory Activity:

a1

Spectrophotometric Assay: Spectrophotometric assays for the HCV serine protease was performed on the inventive compounds by following the procedure described by R. Zhang *et al*, *Analytical Biochemistry*, 270 (1999) 268-275, the disclosure of which is incorporated herein by reference. The assay based on the proteolysis of chromogenic ester substrates is suitable for the continuous monitoring of HCV NS3 protease activity. The substrates were derived from the P side of the NS5A-NS5B junction sequence (Ac-DTEDVVX(Nva); SEQ ID NO: 1), where X = A or P) whose C-terminal carboxyl groups were esterified with one of four different,

a2

Please replace the last full paragraph of page 195 with the following:

Evaluation of Inhibitors and Inactivators: The inhibition constants (K_i) for the competitive inhibitors Ac-D-(D-Gla)-L-I-(Cha)-C-OH (27; SEQ ID NO: 2), Ac-DTEDVVA(Nva)-OH (SEQ ID NO: 3) and Ac-DTEDVVP(Nva)-OH (SEQ ID NO: 4) were determined experimentally at fixed concentrations of enzyme and substrate by plotting v_o/v_i vs. inhibitor concentration ($[I]_o$) according to the rearranged Michaelis-Menten equation for competitive inhibition kinetics: $v_o/v_i = 1 + [I]_o/(K_i (1 + [S]_o/K_m))$, where v_o is the uninhibited initial velocity, v_i is the initial velocity in the presence of inhibitor at any given inhibitor concentration ($[I]_o$) and $[S]_o$ is the substrate concentration used. The resulting data were fitted using linear regression and the resulting slope, $1/(K_i(1+[S]_o/K_m)$, was used to calculate the K_i value.

a3

Please replace the second full paragraph of page 197 with the following:

The BFP-5A/5B-GFP reporter gene contains the BFP and GFP autofluorescent protein coding sequences (Quantum Biotechnologies, Inc., Montreal, Canada) separated by the NS5A/5B cleavage recognition sequence, cloned between the Nhe I and Bam HI restriction endonuclease sites of the pQBI25 cloning vector (Quantum Biotechnologies, Inc.). Expression of the fusion protein is under the control of the CMV IE promoter-enhancer. The bovine growth hormone p (A) sequence of the vector provides the polyadenylation signal for the mRNA. The NS5A/5B cleavage sequence is: SSGADTEDVVCCSMSYTWTGALVTP (SEQ ID NO: 5). DNA sequencing was used to validate the clone.

REMARKS

Entry of the foregoing Amendment is requested. The Amendment inserts sequence identifiers next to each peptide mentioned in the specification. These are only formal changes which do not add any new matter to the present Application and are being done at the request of the Examiner.